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Your Ref:
Our Ref: AFB/JAS/JS/P10272WO

20th January 2006

Dear Sirs,

International Patent Application No. PCT/GB2005/000415
"A Pharmaceutical Composition"
Tillotts Pharma AG *et al*

We refer to the combined International Search Report and Written Opinion ("ISR/WO") issued by the ISA on 3rd November 2005.

Please note that the Authorised Representative for the above mentioned application has changed. Please ensure that all future correspondence regarding this application is marked for the attention of the undersigned.

We hereby request International Preliminary Examination ("IPE") of the above mentioned application. In support of this request, we file herewith a Demand for IPE, duly completed as required. Please debit the required official fee from our deposit account No. 28050163.

We file herewith new pages 12 to 15 to replace the like-numbered pages currently on file, together with an underline/strikethrough version of Claims 1 to 34 as filed indicating the proposed amendments. The Examiner is requested to take into consideration during IPE new Claims 1 to 29 filed herewith on the new pages, together with the following argumentation.

Claim Amendments

Claim 1 has been amended to specify that the pharmaceutical formulation comprises at least one omega-3 polyunsaturated fatty acid in free acid form. Support for this amendment can be found in Claim 12 as filed.

The scope of Claim 11 as filed is not compatible with that for new Claim 1. Thus, Claim 11 as filed has been deleted.

Claim 12 as filed has been deleted as it is redundant over new Claim 1. Claim 13 to 25 have been renumbered as new Claims 11 to 23 and their dependencies changed accordingly.

Claim 23 as filed (new Claim 21) has been amended to the proper "Swiss" form.

Claim 25 as filed (new Claim 23) has been amended to bring the wording of the claim into line with that for new Claim 1.

Claims 26 and 27 as filed have been deleted. Claim 28 as filed has been renumbered as new Claim 24.

Claim 28 as filed (new Claim 24) has been amended to bring the wording of the claim into line with that for new Claim 1 and to incorporate the feature of Claim 29 as filed. Claims 30 to 34 as filed has been renumbered as new Claims 25 to 29 and their dependencies changed accordingly.

Claim 30 as filed (new Claim 25) has been amended to bring the wording of the claim into line with that for new Claim 1.

No further amendments have been made to the claims at this time.

Argumentation

The Search Examiner appears to believe that a "microcapsule" (in which the coating is gelatin) is a type of "soft gelatin capsule". With respect, this is not correct. The skilled person would understand that a "soft gelatin capsule" is not merely a capsule of *any* size made from soft gelatin. In contrast, he would understand that "soft gelatin capsule" is a term of the art referring to unit dosage form of the pharmaceutical formulation.

A "microcapsule" is not a unit dosage form. "Microencapsulation" is a process by which tiny particles of a gas, liquid or solid active ingredient are packaged within a second material for the purpose of shielding the active ingredient from the surrounding environment. "Microcapsules" are an intermediate product as a *plurality* of microcapsules would be used to make a unit dosage form.

As the expression suggests, "microcapsules" are very small in size in comparison to "soft gelatin capsules". In this connection and according to the enclosed pamphlet by Microtek Laboratories, Inc. entitled "Microencapsulation", microcapsules range "...from less than one micron to several hundred microns in size...", which is considerably smaller than a "soft gelatin capsule". In addition, "microcapsules" usually have a thin porous shell so that the entrapped active can readily migrate out of the microcapsule. The thin porous shell is not a good oxygen barrier compared to the shell of a "soft gelatin capsule". Due to their size and volume, "soft gelatin capsules" must have a shell that is much thicker than the shell of a "microcapsule". Thus, the ratio of shell surface to active ingredient volume for a "soft gelatin capsule" is very different from that for a "microcapsule".

As discussed in further detail in the enclosed pamphlet, "microcapsules" are usually manufactured in a bulk emulsion by aqueous phase separation (coacervation) or similar processes

which results in a range of sizes of microcapsule. In contrast, "soft gelatin capsules" are made by a rotary die process in which individually made units are filled with a uniform amount of pharmaceutical formulation and cut from the gelatin ribbon.

With the foregoing comments in mind, the skilled person would not consider a microcapsule to be an example of a "soft gelatin capsule".

None of the prior art cited in the ISR/WO discloses:

- a *soft gelatin capsule* containing a pharmaceutical formulation comprising at least one omega-3 polyunsaturated fatty acid *in free acid form* in which the capsule comprises gelatin extracted by an extraction process comprising *acid* pre-treatment of a collagen source;

- use of at least one omega-3 polyunsaturated fatty acid *in free acid form* in the manufacture of such a soft gelatin capsule for the treatment of chronic inflammatory conditions, hyperlipidaemia, hypertriglyceridaemia, asthma, bipolar disorder or neoplastic disease; or

- a process for the manufacture of such a soft gelatin capsule in which a pharmaceutical formulation comprising at least one omega-3 polyunsaturated fatty acid *in free acid form* is encapsulated in gelatin extracted by an extraction process comprising *acid* pre-treatment of a collagen source.

Therefore, the present invention as defined in new Claims 1 to 29 is novel over the prior art cited in the ISR/WO.

It is asserted that the invention as defined by the new claims also has an inventive step over the prior art cited in the ISR/WO, not least because the significant increase in stability of the soft gelatin capsules containing at least one omega-3 polyunsaturated fatty acid in free acid form, when compared to similar capsules made from Type B bovine gelatin, could not possibly have been predicted before the priority date of the present application.

We look forward to receiving the International Preliminary Examination Report in good time before 13th June 2006 so that our client has sufficient time to consider the report before deciding whether to enter the national phase.

Yours faithfully,

STONES, James Alexander
Authorised Representative

Encls: